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The Interaction of Water-Soluble Pillar[5]Arenes Containing Amide and Ammonium Fragments with Lipid Bilayer

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Abstract
The absence of toxic properties and genotoxic activity was shown for water-soluble pillar[5]arenes containing amide and ammonium fragments. There was no induced mutation associated with the substitution of base pairs in the Ames test. Using the methods of turbidimetry and transmitting electron microscopy (TEM), the interaction of the macrocycle with the surface of lipid bilayer in the liquid crystalline state was established. DLS detected the appearance of larger particles upon titration of liposome suspension with pillar[5]arene **3**. TEM confirms an increase in the average diameter of liposomes in the presence of the macrocycle which may result from liposome fusion.

Keywords Pillar[5]arene · Self-assembly · Toxicity · Macrocyclic receptors

1 Introduction

The development of new systems of molecular recognition is one of the promising areas of modern supramolecular chemistry [1–3]. In recent years, the research of a new class of paracyclophanes—the Pillar[n]arenes—has attracted considerable interest [4, 5]. Pillar[n]arenes are constructed by hydroquinone units (5 to 10) linked in the para position. They are structurally similar to the calixarenes and cucurbiturils that play an important part in host-guest chemistry. Synthetic accessibility and a relatively easy functionalization of the pillar[n]arenes allow one to construct new receptors with predefined properties, such as macrocyclic platform polarity and water solubility [6, 7]. However, little information on the toxicity of such compounds is available [8].

Pillar[5]arene as homolog, obtained with a high yield and known properties [5], is able to form inclusion complexes with various biologically important substrates [8]. In this connection, it is particularly interesting to study the interactions of functionalized water-soluble pillar[5]arenes with the bilayer of the model membrane for determining the ability of these macrocycles to act as agents for targeted delivery of drugs.

As the objects of investigation, we chose water-soluble piliar[5]arenes containing secondary amide, quaternary ammonium, and tertiary amino groups in their structure (Fig. 1). The choice of objects was stipulated by the presence of amide groups, which could form both inside and intermolecular hydrogen bonds, capable of participating in complexation processes. This will increase the affinity of the resulting receptor to various therapeutic agents, and will also allow us to study the processes of self-association and aggregation in the presence of various drugs.

2 Experimental

2.1 Materials and Methods

The water-soluble pillar[5]arenes 4,8,14,18,23,26,28,31,32,35-decakis-[(N-(3′,3′-dimethylaminopropyl)-carbamoylmethoxy]-pillar[5]arene **(1)**, 4,8,14,18,23,26,28,31,32,35-decakis-[(N-(3′,3′,3′-trimethylammoniumpropyl)-carbamoylmethoxy]-pillar[5]arene decachloride (**2**), and

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